REMARKS

Reconsideration of this application is respectfully requested. The specification has been amended to correct a typographical error on page 31. Claim 2 has been restored to the form presented in the February 10, 2009 Amendment. No new matter has been added by way of these amendments. Claims 2, 12, 13, and 17-22 are pending and at issue.

Telephonic Interview with Supervisory Patent Examiner Marschel and Examiner Hughes

Applicant's representatives, Shelly Fujikawa and the undersigned attorney, appreciate the courtesies extended by Supervisory Patent Examiner Marschel and Examiner Hughes during the March 4, 2010 telephone interview. Applicant's representatives agreed to remove the amendments to claim 2 presented in the July 20, 2009 Amendment, and restore the claim to the form presented in the February 10, 2009 Amendment. With respect to the obviousness rejections, Applicant's representatives pointed out (i) that prior to the present invention, it was unknown that a particular metabolite of anagrelide (3-hydroxy anagrelide) greatly aggravated cardiovascular side effects of orally administered anagrelide, (ii) there were numerous other possible causes of the cardiovascular side effects including the PDE-III inhibitory activity of anagrelide itself, and (iii) the surprising discovery that 3-hydroxy anagrelide has much greater potency as a PDE-III inhibitor compared to anagrelide. The Examiners advised that they would reconsider the rejection in view of these arguments and the record as a whole.

Specification Objection

The Examiner has objected to the specification because the structure of anagrelide at the top of page 31 is missing a double bond in its central ring. This typographical error has been corrected. Accordingly, Applicant respectfully requests withdrawal of this objection.

Written Description Rejection

Claims 2, 12-13 and 17-22 have been rejected for failure to comply with the written description requirement. According to the Examiner, the subject matter added to the claims by the July 20, 2009 response including steps (b), (d), and (e) of claim 2 is new matter.

Applicant has restored claim 2 to the form presented in the February 10, 2009 Amendment. Accordingly, Applicant respectfully requests withdrawal of this rejection.

Obviousness Rejections

Claims 2, 12, and 17-20 have been rejected as obvious over Lang in view of Miranda, D'Angelo, and Solberg, as evidenced by Bonkovsky and Ammar.[1,2] Claims 21 and 22 have been rejected as obvious over Lang in view of D'Angelo and Ferrini.[3] The Examiner argues that it would have been obvious to administer anagrelide to treat thrombocythemia in view of Lang, and to administer it transdermally in view of the remaining references.

Applicant respectfully requests reconsideration and withdrawal of these obviousness rejections.

[1] The full citations of these references is as follows: U.S. Patent No. 6,194,420 ("Lang"); U.S. Patent No. 6,221,383 ("Miranda"); U.S. Patent No. 6,024,975 ("D'Angelo"); Solberg, *Seminars in Oncology*, Vol. 28, Issue 3, Supplement 10, page 10-15 (2002) ("Solberg"); Bonkovsky *et al.*, *Zakim and Boyer's Hepatology, 5th Edition*, pages 503-550 (2006) ("Bonkovsky"); and Ammar *et al.*, *International Journal of Pharmaceutics*, Vol. 327, pages 81-88 (2006) ("Ammar").

[2] In the last paragraph on page 4 of the December 10, 2009 Office Action, the Examiner indicates that claim 50 has been rejected. Claim 50 was previously canceled. Applicant has therefore assumed that the rejection of claim 50 is the result of a typographical error.

[3] Ferrini is U.S. Patent No. 5,133,972.

As discussed during the telephonic interview, prior to the present invention it was unknown that the severity of anagrelide's cardiovascular side effects was due to a metabolite (and in particular its 3-hydroxy metabolite). These side effects are not trivial. A large number of patients orally treated with anagrelide fail to tolerate the drug. *See* ¶7 of Dr. Richard Franklin's Declaration submitted on September 19, 2007. The side effects of a drug can be due to a number of causes including the drug itself interacting with (unintended) receptors in the body. Without knowing the cause, a skilled artisan would not have known whether the cardiovascular side effects could be reduced, or how to do so. *See Eibel Process Co. v. Minnesota & Ontario Paper Co.*, 261 U.S. 45, 67-68 (1923) (Eibel discovered that defects in a newsprint paper making machine could be removed by changing the speed of the stock used to make the paper by using gravity. The Supreme Court found that Eibel discovered the problem that caused defective paper, and he then used known principles to fix that problem, stating that "[t]he invention was not the mere use of a high speed or substantial pitch to remedy a known source of trouble. It was the discovery of the source not before known, and the application of the remedy, for which Eibel was entitled to be rewarded in his patent.") .

As none of the cited references disclose or suggest that the severity of the cardiovascular side effects of anagrelide are due to its 3-hydroxy metabolite, a skilled artisan would not have known or expected transdermal administration of anagrelide to significantly reduce these side effects. Accordingly, Applicant respectfully submits that the presently claimed method is non-obvious and respectfully requests withdrawal of this rejection.

CONCLUSION

In view of the above amendments and remarks, it is respectfully requested that the application be reconsidered, that the response be entered, and that all pending claims be allowed and the case passed to issue. If there are any other issues remaining which the Examiner believes could be resolved through a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

Dated: March 10, 2010

Respectfully submitted,

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